

Figure 1

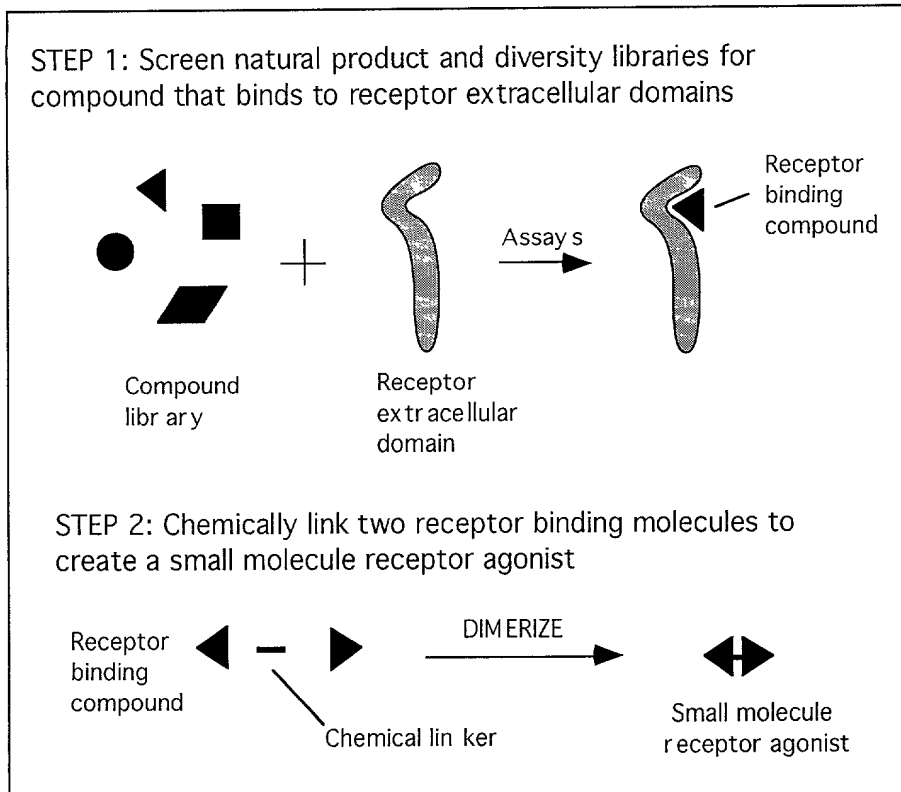


Fig 2: STIMULATION OF IL-2 PRODUCTION BY A SMALL MOLECULE DIMERIZER

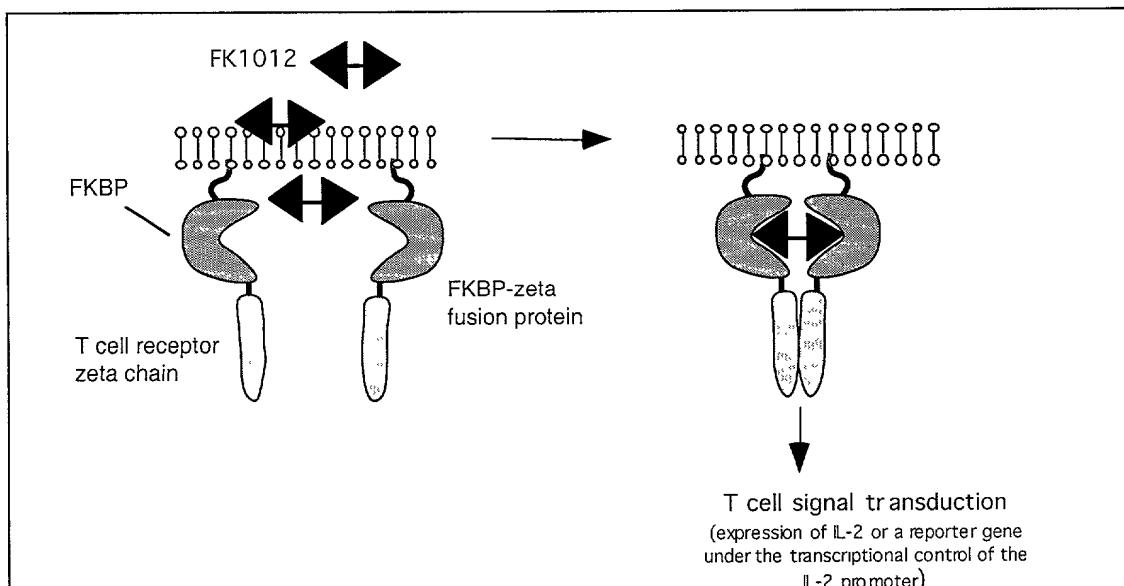


Fig 3: STIMULATION OF ERYTHROPOIETIN RECEPTOR BY A SMALL MOLECULE

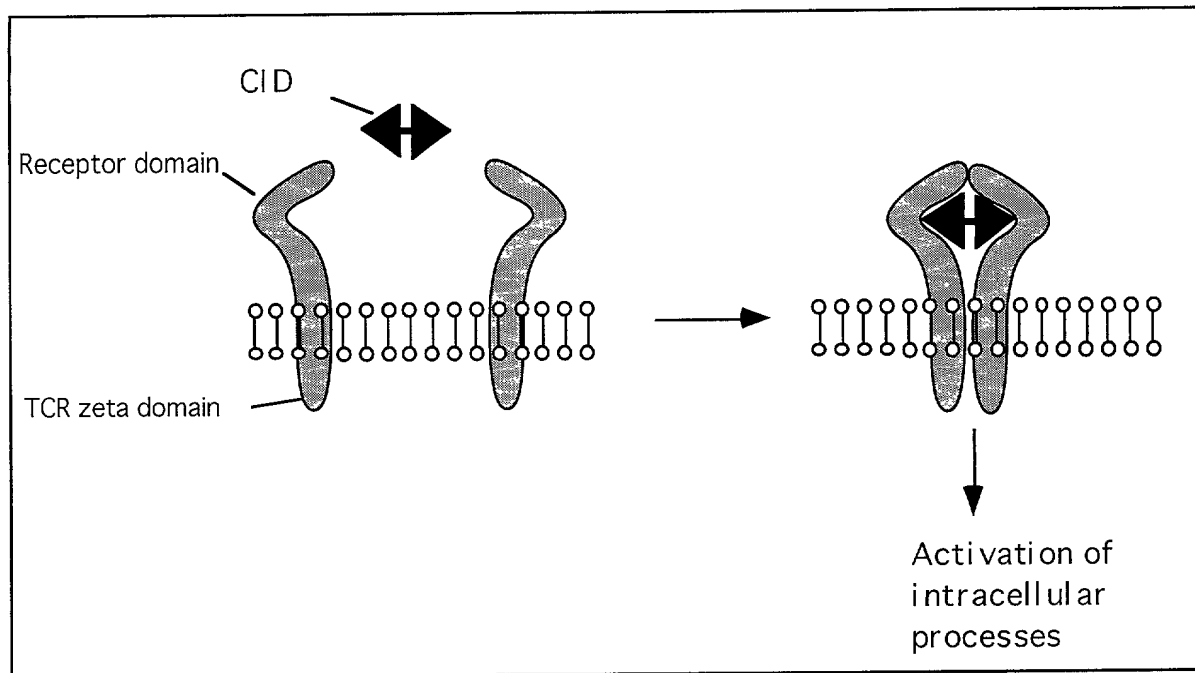


Fig 4: IDENTIFICATION OF RECEPTOR BINDING COMPOUNDS  
USING A COMPETITIVE LIGAND BINDING ASSAY

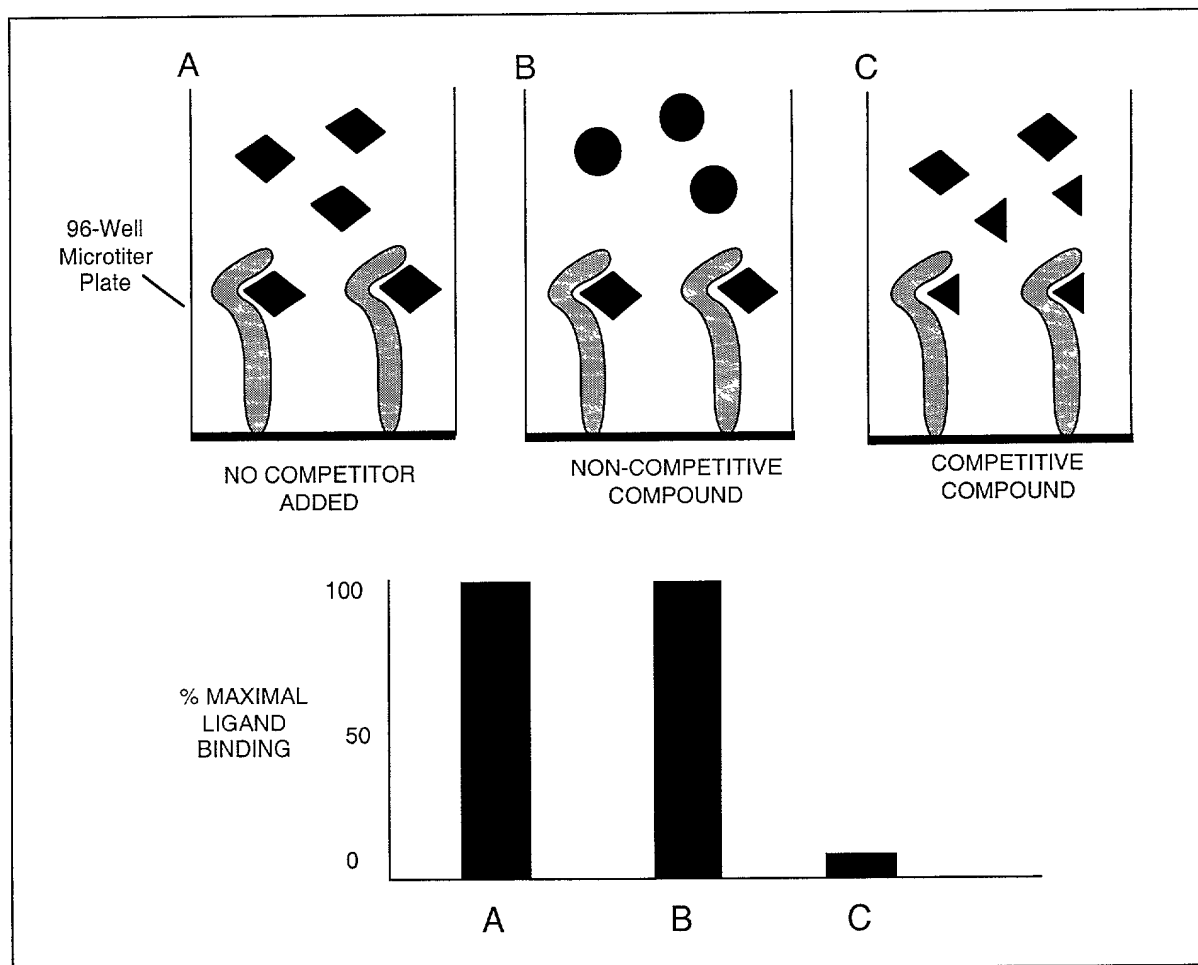


Fig 5: SCREENING MOLECULAR DIVERSITY LIBRARIES FOR COMPOUNDS THAT BIND TO A RECEPTOR EXTRACELLULAR

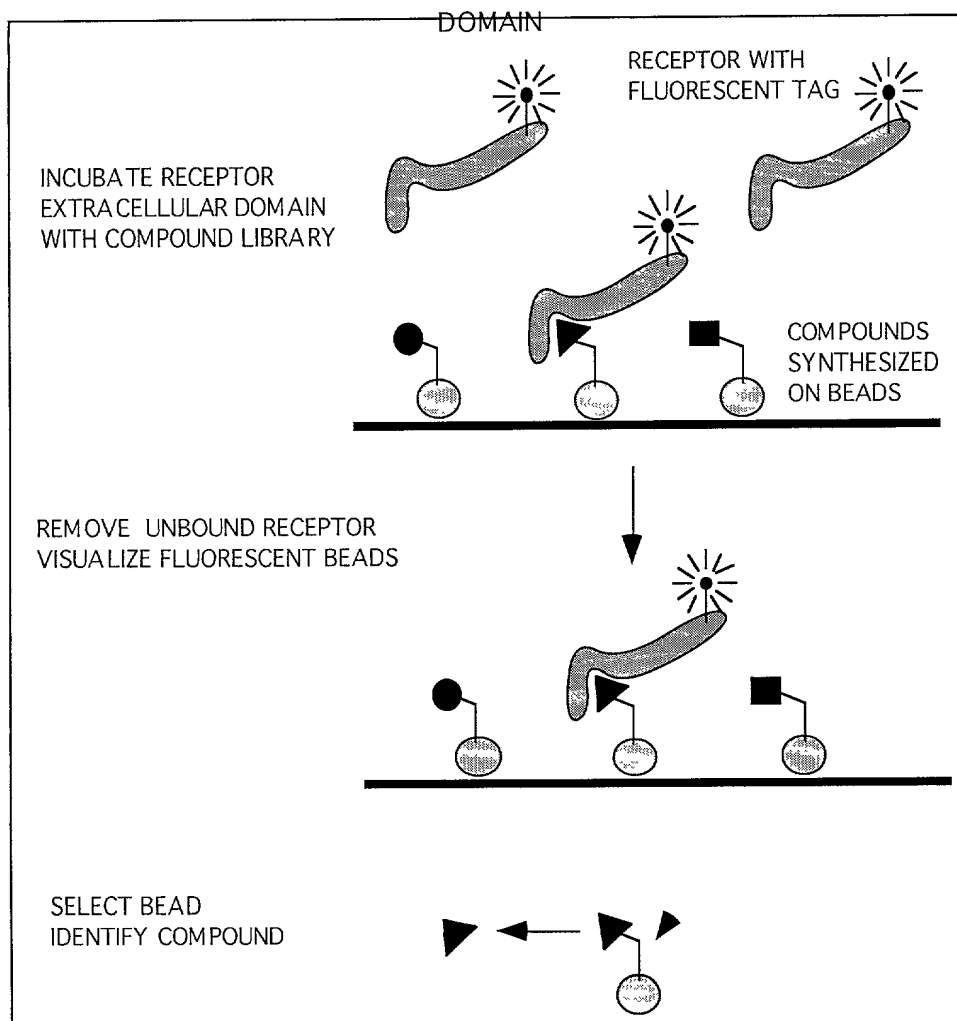
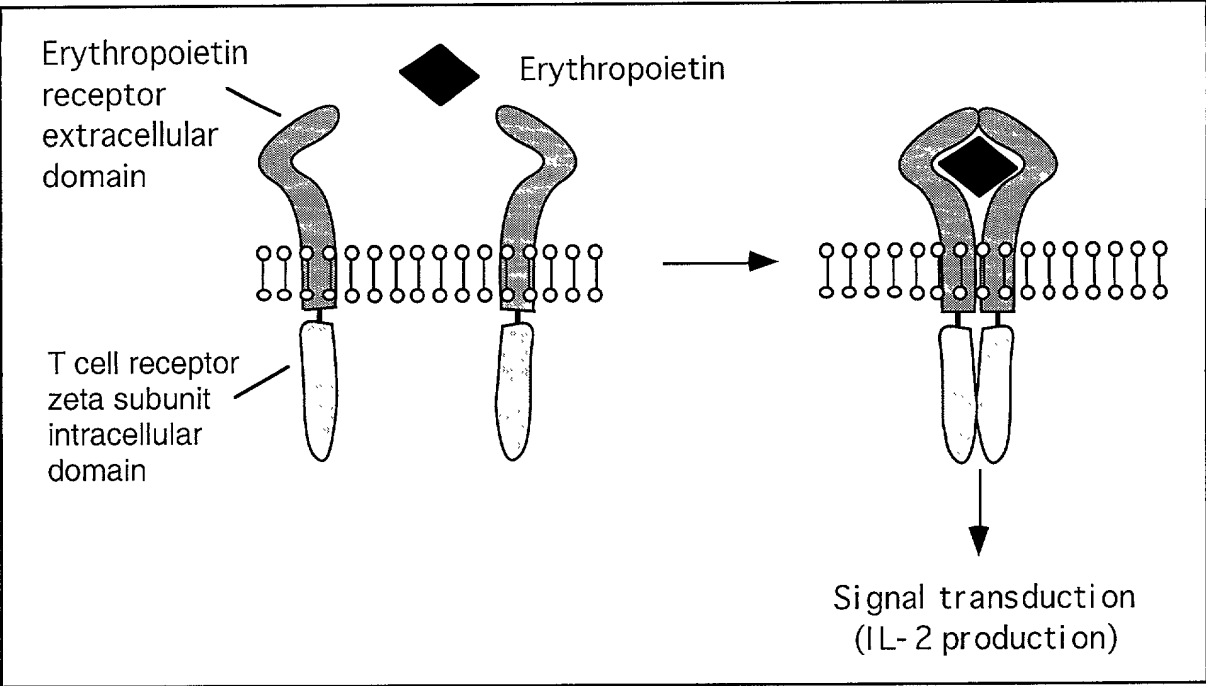


Fig 6: EPO STIMULATES SIGNAL TRANSDUCTION IN AN ENGINEERED CELL LINE



SMALL MOLECULE BLOCKS EPO RECEPTOR-MEDIATED SIGNAL TRANSDUCTION

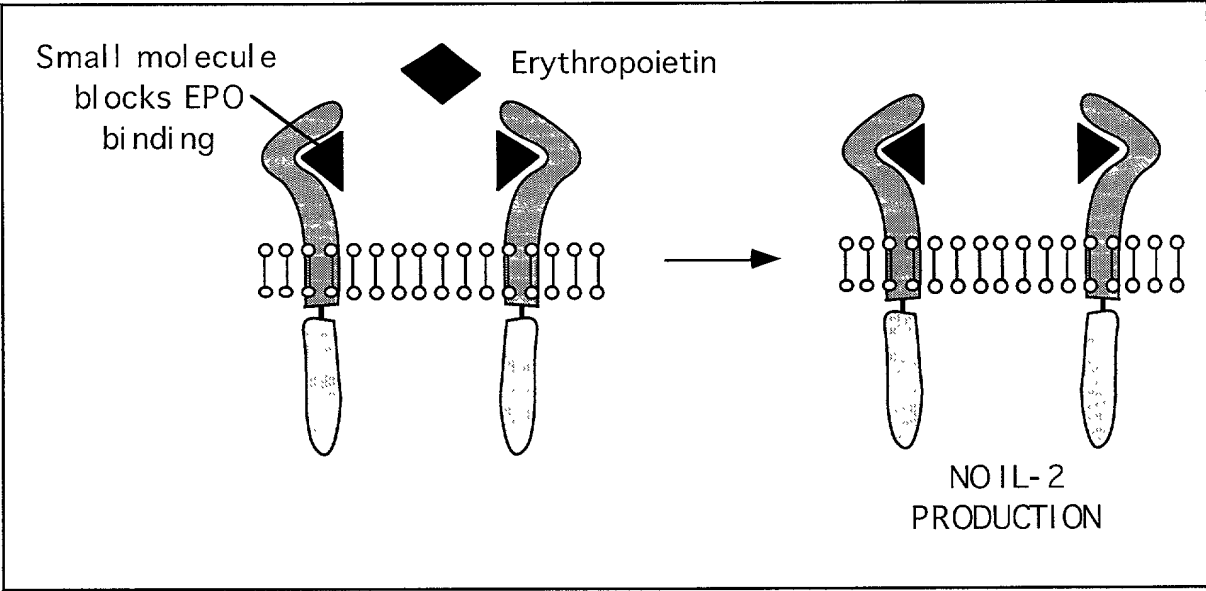
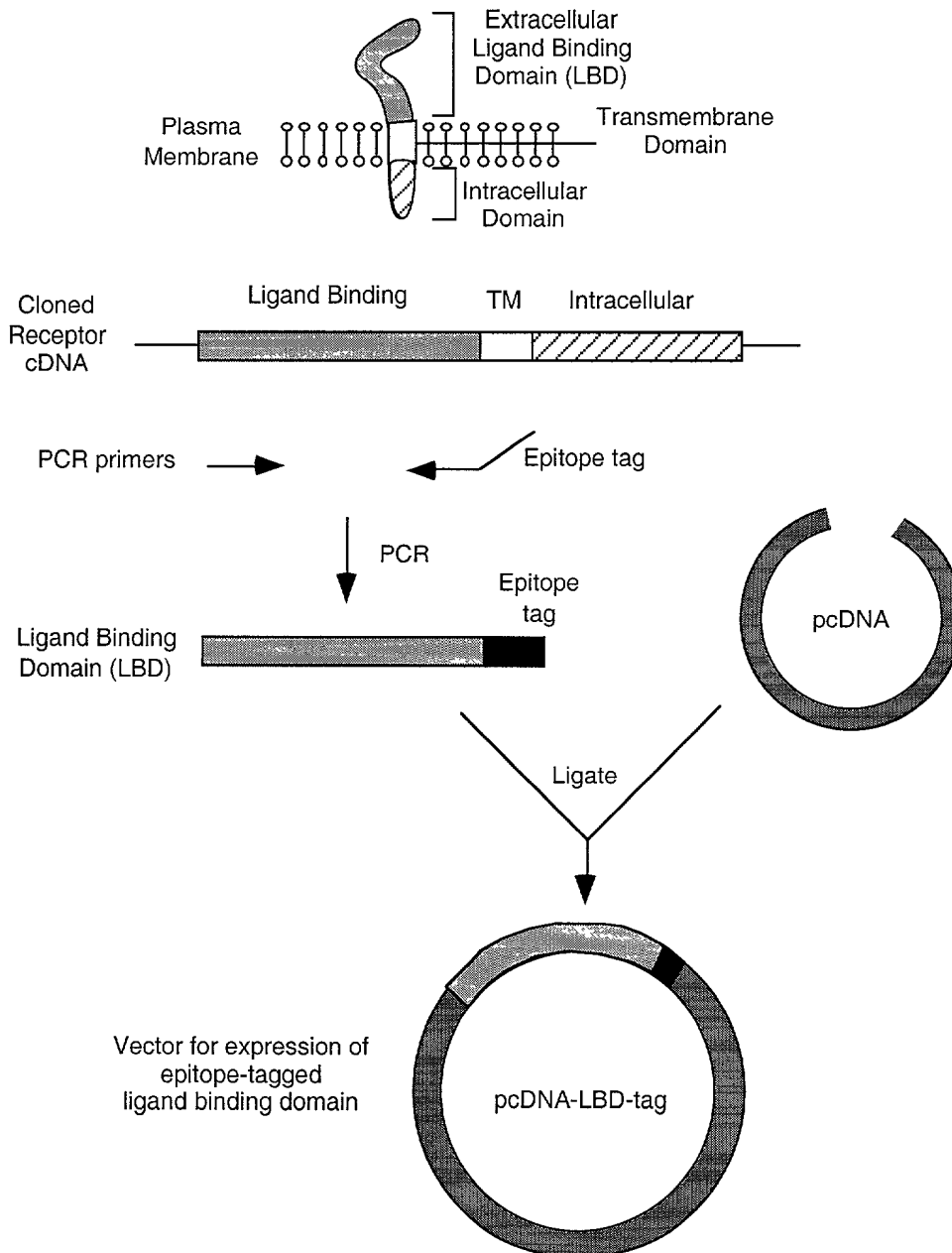


Fig 7: General Method For Construction of Expression Vector for Production of Ligand Binding Domain



The receptor binding domain can be identified by inspection of the receptor coding sequence (e.g. Kyte-Doolittle analysis) or by analysis of deletion mutants (see Watowich et al, Mol. Cell. Biol. 14:3535 1994). PCR primers flanking the LBD are used to PCR amplify the region encoding the LBD. By inclusion of sequences encoding a particular epitope in one or the other PCR primer, an epitope can be fused to the N- or C-terminus of the LBD. Other PCR primers can be used to introduce restriction sites into the ends of the LBD coding sequence to facilitate cloning. The cloned LBD is then ligated into an appropriate expression vector, such as the pcDNA series from Invitrogen, Inc. for mammalian cell expression. To express a receptor-immunoglobulin fusion protein, the amplified LBD segment is ligated into an expression vector containing the hinge, CH2 and CH3 domains of an IgG heavy chain as described in Ashkenazi et al PNAS 88:10535 1991. See e.g., Nature 330, 537- 543 (1987) for details relevant to GH receptor.